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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/037,986	10/18/2001	Larry Gold	NEX01/C8	1060

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EXAMINER
ZITOMER, STEPHANIE W

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 07/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/037,986	GOLD ET AL.	
	Examiner	Art Unit	
	Stephanie Zitomer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *2-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2-02* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Application status

1. The present application is a continuation of multiple ancestral applications dating back to the filing of serial no. 07/714,131, June 10, 1991. However, for prosecution the claims are given the effective filing date of the amendment in which they were presented, February 13, 2002, because the subject matter is not supported by the disclosure for the reasons set forth herein.

Priority claim

2. The paragraph claiming priority is confusing because it does not set forth a straight line of continuation. The insertion of other, related, application numbers is confusing. It is suggested to set out the direct line of continuing applications followed by any further desired information regarding related applications.

Rejection under 35 U.S.C. 112, first paragraph: New matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 2-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to a method for identifying or assisting in identifying the binding site or regulatory region of a nucleic acid binding protein by competing a nucleic acid ligand to a nucleic acid binding protein with DNA or RNA of the binding site region and determining whether the ligand blocks the binding protein from binding to the binding site region thereby assisting in the identification of the DNA or RNA regulatory region. In a passage cited by applicant in support of the claimed subject

matter, the specification mentions that the SELEX method can be used "to assist in the identification and characterization of any binding protein site for DNA or RNA", noting that "[s]uch binding sites function in transcriptional or translational regulation of gene expression" (page 54, line 33-page 55, line 1). In a further cited portion of the specification, proteins known to bind nucleic acids, e.g., polymerases and noncatalytic proteins are mentioned as leading via the SELEX method to "high affinity RNA ligands that bind to the active site of the protein" (page 57, lines 20-25). Finally, in Example 2, also cited by applicant, the ability of a nucleic acid ligand to HIV reverse transcriptase (RT) to inhibit RT activity was tested by competing the ligand with the "starting population", i.e., the candidate mixture of nucleic acids, from which it was concluded that the ligand "either blocks or directly interacts with the catalytic site of the enzyme" (page 81, lines 20-31). In addition to lack of competition with the binding region, it is the enzyme active site which is assessed, not the binding site. Another passage in the specification describes determination of the minimal size of the translational operator, the RNA sequence to which phage T4 DNA polymerase (gp 43) binds. In this experiment the minimal size of the operator was determined by analysis of gp 43 binding to hydrolysis fragments of the operator and sequence determinations were made by assessing binding of gp 43 to operator sequences mutated in the hairpin or loop regions. It was concluded that binding of gp 43 and its transcriptase activity reside in distinct regions of the operator sequence (page 66, lines 15-34). Thus, nowhere in the specification is the claimed method for identifying the binding site of a nucleic acid binding protein via competition with binding region DNA or RNA described. It is suggested that claim 1 might be rewritten according to disclosed methods with the caveat that the patentable utility of a method appearing to serve only for further research would be doubtful.

Rejections under 35 U.S.C. 112, second paragraph: Indefiniteness

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 2-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 2-8 are confusing because the method steps do not lead to a clear "identification" of a "binding site", initially because neither of these is defined. One of ordinary skill in the art would have expected that both the "binding" and "binding region" are nucleotide sequences but this is not clear in the claims and the method steps do not lead to identification of a nucleotide sequence which is the "nucleic acid biding protein's binding site". Clarification is suggested.

(b) The claims are unclear in the recitations "region of a DNA or RNA" and "DNA or RNA region" because "region" is a relative term which is not defined in the claims or in the specification in such a manner that one of ordinary skill in the art would be apprised of the scope of the claimed subject matter. It is suggested to define "binding region" and to clarify its relationship to "binding site", e.g., a binding region comprising a binding site.

(c) In step (c), "added nucleic acid ligand" lacks antecedent basis in "contacting" in step (b). It is suggested to change "contacting" to
--adding--.

(d) Further in step (c), "assists in identifying" and "regulatory region" lack antecedent basis in the preamble and in steps (a) and (b). Clarification is suggested.

(e) In claim 3, "having a similar structure" is confusing as to whether it refers to primary, secondary or tertiary structure and it is unclear how this "similar structure" relates to "identification of the regulatory region". Clarification is suggested.

Rejections under 35 U.S.C. 102(b): Anticipation

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 2, 3 and 5-8 are rejected under 35 U.S.C. 102(b) as being anticipated by the patent to Giordano et al. (5,859,227). Regarding claim 2, the patent discloses the claimed method comprising (a) providing an RNA molecule that interacts with an RNA binding protein, i.e., an RNA ligand to a binding protein (column 11, lines 61-64); (b) contacting the RNA ligand with a mixture of the RNA binding protein and RNA binding region subfragments (column 11, lines 41-43); (c) determining binding protein binding to RNA binding region subfragments and determining the nucleotide sequence of the regulatory region (column 11, line 64-column 12, line 1). Regarding claim 3, the embodiment wherein the RNA binding molecule has a similar structure to the RNA binding region subfragments is disclosed (column 11, lines 23-25). Regarding claims 5-8, the embodiments wherein the RNA binding region is a promoter, an ORI, et al., wherein the protein regulates transcription or translation, and wherein the protein is a transcriptional activator or repressor, a promoter complex member or a translational repressor are disclosed (column 3, lines 1-11).

6. Claims 2, 3, 5, 6 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by the patent to Weissman et al. (5,861,246). Regarding claim 2, the patent discloses the claimed method as follows: the octamer DNA nucleotide sequence, wt-Oct, was known to bind the transcription factor, OctT3, (column 9, lines 22-39) such that the DNA qualifies as the nucleic acid of step (a) in the claim. In step (b), the ligand, wt-Oct, was contacted with a mixture of DNA binding site regions, BS03/9 and BS08, and the DNA binding protein, OctT3 as (wtOct-OctT3 complex) (column 9, lines 40-66). The step (c) determination found that the ligand did not block the protein from binding and one of the binding regions, the BS08 sequence, was the optimal binding sequence for the OctT3 protein (column 9, line 66-column 10, line 3). Regarding claim 3, the embodiment

wherein the ligand and the binding region are similar in structure is disclosed in the competitive binding experiments (column 9, lines 40-64). Regarding claim 5, the embodiment wherein the DNA binding site region is a promoter is disclosed in the patent (column 6, lines 11-19). Regarding claims 6 and 8, the embodiment wherein the protein regulates transcription is disclosed in the patent (column 2, lines 60-62).

Rejection under 35 U.S.C. 102(b)/103(a): Anticipation/Obviousness

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claim 4 is rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Weissman et al. (5,861,246). The patent discloses claim 2 from which claim 4 depends as set forth above at paragraph 5 and further discloses a method for providing a nucleic acid ligand to a DNA binding protein which is essentially the same as that of claim 4 (column 4, lines 36-50). It is not clear in the patent whether the DNA ligand to the DNA binding protein, wt-Oct, was obtained by this method. However, if it was not so obtained, it would have been obvious to the skilled practitioner in the art at the time the claimed invention was made

to use the disclosed method in view of the patent demonstration of its efficacy for providing RNA molecules that bind RNA binding proteins. The skilled practitioner would have been motivated further by his/her obvious familiarity with the routinely practiced SELEX method which was essentially the same as the disclosed method and was well established in the art as the method of choice for obtaining nucleic acids that bind proteins.

Conclusion

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephanie Zitomer whose telephone number is (703) 308-3985. The examiner can normally be reached on Monday through Friday from 9:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152. The official fax phone number for this Group is (703) 308-4242. The unofficial fax number is (703) 308-8724. The examiner's Rightfax number is 703-746-3148.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196. For questions and requests relating to formal matters contact LIE Chantae Dessau at 703-605-1237.

S. Zitomer

Stephanie Zitomer, Ph.D.

June 20, 2003

STEPHANIE W. ZITOMER
PRIMARY EXAMINER